

discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Brobeck, Phleger & Harrison, LLP Deposit Account No. 50-1640.

Respectfully submitted,

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Brobeck, Phleger & Harrison LLP Intellectual Property Department 1333 H Street, N.W., Suite 800 Washington, D.C. 20005 (202) 220-6000

## EXHIBIT A MARKED VERSION OF THE REPLACEMENT PARAGRAPH VERSION OF THE REPLACEMENT PARAGRAPH RATENT APPLICATION SERIAL NO. 09/882,376

Figure 2A illustrates the fluorescence emission spectra of APC at 500 ng/ml where solid line impresents. APC stored for 0 h and the dotted line is APC stored at room temperature for 2 h. Note that at 0 h, the emission maximum was 660 nm while after 2 h the emission shifted to 642 nm and lost 50% of it's fluorescence emission intensity. In Figure 2B the solid line illustrates the fluorescence emission spectra for SL-APC stored at a concentration of 500 ng/ml in PBS for 0 h and the dotted line is the emission spectra of the solution after being stored for 2 h. Similarly, in Figure 2C the solid line illustrates the fluorescence emission spectra for XL-APC stored at a concentration of 500 ng/ml in PBS for 0 h and the dotted line is the emission spectra of the solution after being stored for 2 h.

Figure 3 illustrates the effect of high temperature (65°C) on APC, SL-APC, and XL-APC stability. The graphs illustrates the decrease in % of initial fluorescence or change in relative fluorescence intensity (CPS) (measured at 660 nm) over time when Native APC, SL-APC, and XL-APC when stored at 65°C.

Figure 4 illustrates the emission spectra for GL-APC, when stored in dimethyl sulfoxide at 5 min and 5 days as compared to a control. Additionally, Figure 4 illustrates the emission spectra for XL-APC and SL-APC when stored in dimethyl sulfoxide at 90 min and 5 days as compared to a control.

Figure 5 illustrates the detection of phosphorylated poly-GAT with europium labeled anti-phosphotyrosine IgG (PY20) and SL-APC labeled streptavidin or a commercially available XL-APC labeled streptavidin. Poly-GAT was phosphorylated with a src-tyronsine kinase and then titrated from 0 ng to 12 ng. Positive phosphorylation was measured as a ratio using two wavelengths (620 & 650 nm) as previously described. *See*, Mathis, *Clin. Chem.*, 41:1391-1397, 1995.

Figure 6 illustrates a comparison of two tyrosine kinase inhibitors, staurosporine, and PP-1, on src tyrosine kinase activity measured in a TR-FET assay using SL-APC/Europium chelate as the FRET pair. Figure 7 illustrates the comparison of four europium acceptor dyes (XL-APC, SL-APC, PBXL-3, CryptoFlour-2) for europium chelate emission in a TR-FRET assay titrating the inhibition of  $\beta$ -insulin receptor tyrosine kinase activity with staurosporine (top graph) and 5-iodotubercidin (bottom graph).